Amendments to the Specification

Page 11, line 1, Replace original Table 1 with the following:

Table 1. Consolidated Human p185 HER-2 predicted B cell epitopes listed in the order of ranking by amino acid residue numbers. Asparagine (N)-linked glycosylation sites are underlined in bold.

Predictive Ranking	Residue	Amino Acid Sequence	Secondary Structure
7	27 – 45	Tgtdmklrlpaspethldm, SEQ ID NO: 1	25 – 28 β turn; 29 – 32 α helix; 35 – 38 β turn
8 (DW5)	115 – 136	AVLDNGDPLNNTTPVTGASPGG, SEQ ID NO: 2	116 – 135 β turn
9	168 – 189	LWKDIFHKNNQLALTLIDTNRS, SEQ IDNO: 3	173 – 176 β turn; 177 – 181 α helix
1	182 – 216	TLIDTNRSRACHPCSPMCKGSRCWG ESSEDCQSLT; SEQ ID NO: 4	184 – 212 β turn/loop
6	270 – 290	ALVTYNTDTFESMPNPEGRYT, SEQ ID NO: 5	273 – 286 β turn; 278 – 280 α helix
3	316 – 339	PLHNQEVTAEDGTQRAEKCSKPCA, SEQ ID NO: 6	319 – 324 α helix; 324 – 336 β turn.
10 (DW1)	376 – 395	PESFDGDPASNTAPLQPE, SEQ ID NO: 7	379 – 388 β turn
12 (DW6)	410-429	LYISAWPDSLPDLSVFQNLQ, SEQ ID NO: 8	413-421β turn
2	485 – 503	LFRNPHQALLHTANRPEDE, SEQ ID NO: 9	497 – 500 β turn; 499 – 504 α helix
11	560 – 593	CLPCHPECQPQNGSVTCFGPEADQCVACAH YKDP, SEQ ID NO: 10	561 – 572 & 589 – 593 β turn; 579 – 581 α helix
4	605– 622	KPDLSYMPIWKFPDEEGA, SEQ ID NO: 11	616 – 620 α helix
5 (DW4)	628 – 650	INGTHSCVDLDDKGCPAEQRASP, SEQ ID NO: 12	635 – 642 β turn; 643 – 646 α helix

Page 17, please replace the paragraph beginning on line 27 and extending through line 2 on page 18 with the following:

The polynucleotides encoding the HER-2 B cell epitope, the HER-2 CTL epitope or the chimeric peptides comprising such epitopes are used to express recombinant peptide using techniques well known in the art. Such techniques are described in Sambrook, J. et al (1989) Molecular Cloning A Laboratory Manual, Cold Spring Harbor Press, Plainview, N.Y. and Ausubel, F. M. et al. (1989) ~~Cuurent~~ Current Protocols in Molecular Biology, John Wile & Sons, New York, NY. Polynucleotides encoding the HER-2 B cell epitope, the HER-2 CTL epitope or the chimeric peptides comprising such epitopes are also used to immunize animals.

Page 19, please replace the paragraph beginning on line 19 with the following:

Peptide Synthesis and HPLC Purification. Peptides were synthesized as previously described (Kaumaya 1994). Briefly, peptides were synthesized on a Milligen/Biosearch 9600 peptide synthesizer, using a 4-methylbenzhydrylamine resin as the solid support (substitution 0.54mm/g). The Fmoc/t-butyl synthetic method was employed using 4-(hydroxymethyl) phenoxyacetic acid as the linker. After the final deprotection step, protecting groups and peptide resin bond were cleaved with 90% TFA, 5% anisole, 3% thioanisole, 2% ethanedithiol. Crude peptide was purified by semipreparative HPLC using a ~~Vydac~~ Vydac™ C4 (10mm x 25cm) column at 32.5°C. Buffers were 0.1% TFA in H_20 and 0.1% TFA in acetonitrile. Peptides incorporate a "promiscuous" T cell epitopes MVF 288-302 (Kaumaya 1994): DW1MVF (HER-2 376-395), MVFDW4 (628-647), DW5MVF (115-136), DW6MVF (410-429).

Page 20, please replace the paragraph beginning on line 16 with the following:

Mercuric Acetate. Peptide was dissolved in a minimal amount of water and 100mg/mm S-tBu solution (2- 10 fold excess) added. Peptide was placed under vacuum and precipitated by 2-Mercaptoethanol in a 55°C water bath under stirring. After filtering through dampened ~~Celite~~ Celite™, the filtrate was rotary evaporated, acidified with 0.1% TFA in water and lyophilized.

Page 20, please replace the paragraph beginning on 21 and extending through line 4 on page 21 with the following:

Immunizations and animals. Female New Zealand white rabbits were obtained from Mohican Valley Rabbitry (Loudenville, OH). Rabbits were immunized subcutaneously at multiple sites with a total of lmg of peptide emulsified in CFA. Subsequent booster injections (1mg and 500μg in PBS) were given three and six weeks after the primary immunization. Sera were collected and complement inactivated by heating to 56°C for 30min. Sera aliquots were stored at -5 to -15°C. Antibodies were purified by ammonium sulfate precipitation: A stock solution of saturated ammonium sulfate solution (SAS) was prepared, autoclaved and cooled to 4°C. Antibody was allowed to precipitate by slowly adding SAS to 35% v/v under stirring in

cold room. Samples were centrifuged 14,000 xg 20min and the supemate stored at -20°C. The pellet was dissolved with 0.1M PBS in ½ original volume. Fractions were then placed in ~~Slide-a-lyzer~~ Slide-a-lyzer™ cassettes (Pierce) and dialyzed against frequent changes of >200 volumes pH 8, 0.15M NaCl. The saline was brought to pH 8 with a few drops of 0.1M NaOH. IgG concentration was determined by radial immunodiffusion (RID) (The Binding Site, UK). Monoclonal antibodies were purchased from Oncogene Science.

Page 27, please replace the paragraph beginning on line 8 with the following:

FACS and ~~Immunoprecipitatio~~ Immunoprecipitation: Flow cytometric analysis determined that DW1MVF anti-peptide antibody directly targeted the HER-2 receptor. ~~(See Figure—)~~ (See Figure 3.) A commercially available mouse Mab to HER-2/neu was used as a control in SKBR3 cells. Negative control sera showed no binding to the receptor while an increase in fluorescence was seen with the immune sera. Fluorescence intensity of the polyclonal antipeptide serum was comparable to the monoclonal antibody. Therefore polyclonal serum can mimic the specificity and affinity of monoclonal antibodies.

Page 27, please replace the paragraph beginning on line 27 with the following:

The peptide antibodies MVFDW4, DW5MVF and DW6MVF however did not give the same intensity of fluorescence as DW1MVF. Therefore, immunoprecipitation was used to verify specificity for HER-2. SKBR3 cells were immunoprecipitated with Protein A/G purified antipeptide antibodies. Antibodies are shown to be HER-2 reactive ~~v~~'. Identical bands are evident in the Mab sample and the anti-peptide antibodies.

Page 30, please replace the paragraph beginning on line 9 with the following:

A chimeric peptide comprising a modified sequence 316-339 of the HER-2 protein, the promiscuous helper T cell epitope from measles virus fusion protein (amino acids 288-302) at the N-terminus, and a GPSL, SEQ ID NO: 20, linker (MVFND2) was synthesized using procedures as described in example 1 above. HER-2 sequence 316-339 contains three cysteines at positions 331, 334 and 338. Using molecular modeling software (Hyperchem, Hypercube Inc, Ontario, Canada), we determined that residues 334 & 338 form energetically most stable

cysteine-cysteine bond pair. Hence, during synthesis we substituted Cysteine 331 with Alanine to prevent interference with secondary structure formation and aggregation post synthesis.

Page 31, please replace the paragraph beginning on line 4 with the following:

A chimeric peptide comprising a modified sequence 495-508 of the HER-2 protein, the promiscuous helper T cell epitope from measles virus fusion protein (amino acids 288-302) at the N-terminus, and a GPSL, SEQ ID NO: 20, linker (MVFND3) was synthesized using procedures as described in example 1 above. HER-2 sequence 495-508 is four residues short of an optimal B-cell epitope of approximately 17-18 residues spanning the 750 Angstrom^2 antigen binding site of an antibody. Hence, in order to extend this sequence to fit the antigen-binding pocket better, we looked at the scores assigned to adjacent sequences for their probability to form an antigenic epitope. Sequence 485-499 was assigned the highest score of all sequences analyzed in the HER-2 extracellular domain on Welling's antigenicity scale, this scale indicates the probability of a 5 residue sequence to form an antigenic epitope. This sequence also harbors a defined β-turn (Residues 488-491) and an α-helix (Residues 491-495). Therefore, we extended the originally proposed epitope 495-508 to include 485-499. Furthermore, we shortened the sequence 495-508 by five residues at the C-terminus to exclude the single cysteine at position 504 that could lead to aggregation of the peptide and make it difficult for purification and characterization. The four residues following cysteine do not form any defined secondary. This epitope was linked with the promiscuous T helper cell epitope TT at the C-terminus (See Table 4).

Page 31, please replace the Table legend beginning on line 21 with the following;

Table 4. HER-2 B-cell epitope chimeric constructs incorporating promiscuous helper T cell epitope from tetanus toxoid (TT 580-599) at the C-terminus and a GPSL. SEQ ID NO: 20, linker joining the two epitopes. Also shown is the % homology of the HER-2 B-cell epitope sequences with corresponding sequences in rat NEU. Note: Cys 331 -> Ala 331 change in the construct HER-2 (316-339) TT is underlined.

Page 32, please replace the paragraph beginning on line 2 with the following:

A chimeric peptide comprising amino acids 605-622 of the HER-2 protein, the promiscuous helper T cell epitope from measles virus fusion protein (amino acids 288-302) at the N-terminus, and a GPSL, SEQ ID NO: 20, ~~linker(MVFDN4)~~ linker (MVFDN4) was synthesized using procedures as described above in example 1.

Page 34, please replace the paragraph beginning on line 20 and extending through line 7 on page 35 with the following:

A four-day Elispot protocol was used to detect the INF-γ production of spleen cells. On day 1, Elispot plate (PolyFiltronics) was coated with Anti-mouse-INF-γ (clone R4-6A2, Pharmingen) diluted in sterile PBS with no azide at 4 μg/ml. The plate was then incubated overnight at 4°C in a humidity chamber. On day 2, the plate was washed with PBS four times and then blocked with 1% BSA in DMEM with no additives at 200 μl/well for 1 hour at room temperature. After BSA was removed, fresh spleen cells harvested into HL-1 ~~medium(Biowhittaker)~~ medium (Biowhittaker) with 1% L-glutamine were added to wells at a certain concentration. The plate was then incubated in humidified incubator at 37°C, 5% $C0_2$ for 24 hours. On day 3, after cells were removed and plate washed with PBS once, the plate was further washed with PBS/Tween 20(2000:1) four times. Biotinylated anti-INF-γ (clone XMG 1.2, Pharmingen) diluted in PBS/Tween 20/1% BSA to 2 μg/ml was added into wells at 100μl/well. The plate was incubated at 4°C overnight in a humidity chamber. On day 4, after the plate was washed with PBS/Tween 20 four times, goat anti-biotin/alkaline phosphatase conjugate(Vector Laboratories Inc.) 1:1000 diluted in PBS/Tween 20/1% BSA was added at 100 μl/well. The plate was incubated at room temperature for 2 hours, washed with PBS four times. BCIP/NBT alkaline phosphatase substrate(Kirkegaard and Perry Laboratories Inc.) was added at 200μl/well for incubation at room temperature. The reaction was quenched in running tap water when spots were visualized on the plate. The plates were air dried prior to reading the spots.